PORTAL HAEMODYNAMICS AS A PREDICTOR OF OESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS

DISSERTATION SUBMITTED FOR

DM MEDICAL GASTROENTEROLOGY

BRANCH- IV

AUGUST 2012

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY CHENNAI , TAMILNADU

CERTIFICATE

This is to certify that this dissertation entitled **"PORTAL HAEMODYNAMICS AS A PREDICTOR OF OESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS"** submitted by **R. SENTHIL KUMAR** to the faculty of Medical Gastroenterology, The Tamilnadu Dr. MGR Medical University, Guindy, Chennai-600032 in partial fulfillment of the requirement for the award of DM Degree, Branch IV (Medical Gastroenterology) is a bonafide work carried out by him under my direct supervision and guidance.

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ACKNOWLEDGEMENTS

I am greatly indebted to my guide **Dr.S.Jeevan Kumar, M.D.**,**D.M.,** Professor of Medical Gastroenterology, Department of Digestive Health and Diseases, Govt.Kilpauk Medical College, Chennai, for giving a chance to undertake this dissertation work under his guidance. Also I express my deep sense of gratitude for his encouragement, directions, periodical discussions, rigorous reviews and precious suggestions for shaping my dissertation. I also thank him for giving me the permission to do this dissertation in Govt. Peripheral Hospital, Anna nagar, Chennai-102.

I express my gratitude to **Dr.P.Ganesh, M.D.**,**D.M.,** Associate Professor, Department of Digestive Health and Diseases, Govt. Kilpauk Medical College, for his kind encouragement and review of my work, besides providing me with all the required facilities.

I am extremely grateful to **Dr.P.Ramakrishnan, M.D.,D.L.O,** Dean, Govt. Kilpauk Medical College for granting me the permission to do this dissertation in Kilpauk Medical College Hospital, Chennai.

I am very much thankful to **Dr.P.Gopinath, M.D.,** Assistant professor, Department of Radiology, who has guided me a lot in doing this dissertation.

I am extremely thankful to **Dr.R.Balamurali, M.D.,D.M., Dr.G.Ramkumar, M.D.,D.M., and Dr.K.Muthukumaran, M.D.,D.M.,** Assistant Professors in the Department of Digestive Health and Diseases, who have guided me a lot.

I am thankful to my colleagues Dr. T.Arun M.D., Dr. P.Jagadesan M.D., Dr. B.Prakash Shankar M.D., Dr. A.R.Akilandeswari M.D., Dr. Jayakumar jayakrishnan M.D., Dr.R.Poppy Rejoice M.D., Dr. G.Sathya M.D., Dr.A.Senthil vadivu M.D., Dr.R.Vinoth Kumar, M.D., Dr.S.Mukundan M.D., Dr.V. Anand M.D.,Dr.P. Thirumal M.D., Dr.A.Santi selvi M.D., Dr.M.Tarakeshwari M.D.,Dr. D.Babu vinish M.D., who have helped me a lot in this dissertation.

I am extremely thankful to Dr.R.Ravanan Ph.D., Associate professor, Department of statistics, Presidency college, Chennai – 5, for his help in the statistical analysis of my dissertation work.

I thank all the referring institutions and doctors for their trust and timely referral of needy patients to our department. I thank all the patients who have ungrudgingly lent themselves to undergo this study, without which this study would not have seen the light of the day.

I also thank all the paramedical staffs of Govt. Peripheral Hospital, Anna nagar for their help.

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ABSTRACT

AIM

To evaluate the relationship of Doppler parameters of hepatic and portal vasculature, hepatic vein wave forms with presence and size of oesophageal varices in cirrhotic patients.

MATERIALS AND METHODS

A cohort of cirrhotic patients identified by clinical, laboratory and radiological parameters were evaluated. They were investigated for oesophageal varices by oesophagoduodenoscopy and by Doppler ultrasound. The relation between the presence and size of oesophageal varices and Doppler parameters were studied.

RESULTS

Fifty two patients were enrolled in this prospective study. There were 44 male and 8 female patients. 23 patients were in Child Pugh Class C , 16 in Child Pugh Class B and 13 in Child Pugh Class A.Small oesophageal varices were associated with monophasic wave forms in 19.4%. biphasic wave forms in 38.7%, triphasic wave forms in 41.9%. Large oesophageal varices were associated with monophasic wave forms in 42.1%. biphasic wave forms in 52.6%, triphasic wave forms in 6.3%. The p- value was statistically significant with 0.013 [$p < 0.05$].Spleen size greater than 15.3 was associated with large oesophageal varices which was statistically significant. Except for splenic artery resistivity index, none of the other Doppler parameters were statistically significant for large oesophageal varices.

CONCLUSION

Our study data suggested that monophasic hepatic vein wave forms, splenic artery resistivity index, and spleen size greater than 15. 3 cms were related with presence of large oesophageal varices.These parameters may help in targeted identification of patients with large oesophageal varices and aid in their management.

KEY WORDS: Cirrhosis, Doppler ultrasound, Hepatic vein wave forms, Oesophageal varices.

INTRODUCTION

Portal hypertension is the most common and dreaded complication of chronic liver disease. It is responsible for the development of gastroesophageal varices, variceal hemorrhage, ascites, renal dysfunction, portosystemic encephalopathy, hypersplenism, and hepatopulmonary syndrome. Bleeding from ruptured oesophagogastric varices is a major complication of portal hypertension and a frequent cause of death. Only 40% of Child pugh class A patients have varices, while they are present in 85% of Child pugh class C patients[1].

In the cirrhotic patients without varices at first endoscopy, the annual incidence of new varices is at mean of 7%, ranging from 5 to 10%[2]. A hepatic venous pressure gradient over 10 mm Hg is the strong predictor for the development of oesophageal varices. Once developed, varices progress in size from small to large before they eventually rupture and bleed. Studies assessing the progression from small to large varices have showed rates of progression of varices ranging from 5 to 30% per year.[3]

Changes in hepatic vein pressure gradient (either spontaneous or caused by drug therapy or transjugular intrahepatic porto systemic shunts) are usually accompanied by parallel variations in the size of the oesophageal varices, which is significantly reduced when HVPG decreases below 12 mm Hg.[4]

Oesophageal variceal bleeding related to portal hypertension is the second most common cause of severe upper gastrointestinal bleeding (after peptic ulcer disease). The acute mortality rate with each bleed is approximately 30%, and the long-term survival rate is less than 40% after one year with medical management alone. Despite advances in medical therapy, endoscopic hemostasis and portosystemic shunt procedures overall long-term survival rates have not improved for patients with variceal bleeding. Liver transplantation, however can improve the survival in selected patients. Survival in nontransplanted patients with variceal bleeding is heavily influenced by the severity of underlying liver disease, with poorer survival rates for patients with Child-Pugh class C cirrhosis than for those with Child class A or B cirrhosis.

A combination of beta blockers and variceal band ligation is probably the best treatment option, especially in patients who have bleeding. Patients who rebleed despite combined endoscopic and pharmacologic treatment may be treated by transjugular intraheptic or surgical portosystemic shunting. TIPS is the only option in nonsurgical candidates. All Child–Pugh class C patients should be considered for liver transplantation.

The role of non invasive markers in prediction of oesophageal varices in patients with cirrhosis was evaluated in various studies[5] . However, the usefulness of these markers in clinical use is still unclear. Doppler ultrasonography allows us to examine haemodynamics of abdominal vessels including the hepatic and portal system. Thus, many investigators have attempted to confirm the usefulness of Doppler ultrasound in assessing portal hypertension in cirrhotic patients. In particular, it would be highly desirable to have any Doppler parameter be a suitable substitute for the invasive current gold standard of measuring hepatic venous pressure gradient for assessing portal hypertension.

Predicting the grade of varices by noninvasive methods at the time of diagnosis is likely to predict the need for prophylactic beta blockers and band ligation as treatment for the varices. Therefore the present study has been undertaken to determine the appropriateness of Doppler parameters of portal vasculature and hepatic vein wave forms in predicting the existence and grading of the oesophageal varices.

REVIEW OF LITERATURE

PORTAL HYPERTENSION

Portal hypertension is defined as a pathologic increase in the portal venous pressure gradient between the portal vein and the inferior vena cava. In patients with cirrhosis, portal hypertension results from changes in portal resistance in combination with changes in portal inflow. The influence of flow and resistance on pressure can be represented by the formula for Ohm's law:

P (Pressure) = Q (Blood flow) × R (Resistance)

Increase in portal resistance or portal flow contribute to increased portal pressure. Portal hypertension always results from increase in both portal resistance and portal flow. The mechanism of the increase in portal resistance depends on the site and cause of portal hypertension. Due to increase in hepatic resistance and the decrease in hepatic compliance, small changes in flow that do not increase pressure in the normal liver can have a prominent stimulatory effect on portal pressure in the cirrhotic liver.

The increase in portal venous inflow is a part of a generalized systemic derangement termed the hyperdynamic circulatory state. Collateral vessels that dilate and new vascular sprouts that form connect the high pressure portal venous system with low pressure systemic veins. Unfortunately, this process of new vessel formation and collateralization is insufficient for normalizing the portal pressure and actually causes complications of portal hypertension, such as oesophageal varices. Approaches to block this angiogenic process are a compelling target for drug development.

The changes in portal flow and resistance can be viewed as originating from combination of mechanical and vascular factors. Mechanical factors include the fibrosis and nodularity of the cirrhotic liver with distortion of the hepatic vascular architecture and the remodelling that is recognized to occur in the systemic and splanchnic vasculature in response to the chronic increase in flow and shear stress that characterize the hyperdynamic circulatory state.

Vascular factors include intrahepatic vasoconstriction, which contributes to increased intrahepatic resistance, and the splanchnic and systemic vasodilatation that accompanies the hyperdynamic circulatory state. The vascular factors that contribute to portal hypertension are

particularly important because they are reversible and dynamic and therefore compelling targets for experimental therapies . Conversely, effective therapies for the fixed, mechanical component of portal hypertension caused by scar, regenerative nodules, and vascular remodelling are currently lacking. Indeed, most available therapies for portal hypertension focus on correction of hemodynamic alterations in the portal circulation.

A decreased intrahepatic availability of vasodilatory nitric oxide due to decrease in its production with combination of an increase in the production of the endothelin-1 which is a potent vasoconstrictor, is the major cause of increase in hepatic vascular resistance[4]. Cirrhosis is a hyperdynamic circulatory state that is characterized by peripheral and splanchnic vasodilation, reduced mean arterial pressure, and increase in cardiac output. Nitric oxide mediated splanchnic vasodilatation produces an increase in increase in portal pressure[6].

Portal pressure is most commonly determined by the hepatic vein pressure gradient (HVPG), which is the difference between the wedged hepatic venous pressure (WHVP) which reflects the hepatic sinusoidal pressure and free hepatic vein pressure (FHVP). The HVPG is increased in intrahepatic causes of portal hypertension, but remains normal in

prehepatic causes of portal hypertension. The normal value of hepatic vein pressure gradient is three to five mm Hg.

The natural history of cirrhosis can be divided into a preclinical phase and a subsequent clinical phase. The preclinical phase is usually prolonged over several years; once decompensatory features such as the development of ascites, encephalopathy, and variceal bleeding occur, the remaining course of the disease is much more shorter and usually fatal. Portal hypertension is crucial in the transition from the preclinical phase to the clinical phase of cirrhosis. It is an important mechanism for formation of ascites and encephalopathy and is a direct cause of variceal bleeding and bleeding-related death.

From a clinical standpoint, oesophagogastric varices are the most important collateral vessels. They tend to increase in size with the increase of portal pressure and rupture when wall tension exceeds a critical value. Knowledge of the natural history of portal hypertension is crucial in making important decisions about the diagnosis, monitoring and follow-up, and treatment of patients with this condition.

Portal hypertension is classified according to the localization of the flow resistance as pre hepatic, intrahepatic and post hepatic causes.

The intra hepatic form of portal hypertension is further subdivided into pre sinusoidal , sinusoidal and post sinusoidal portal hypertension

NON – PARENCHYMATOUS PORTAL HYPERTENSION

1. PREHEPATIC PORTAL HYPERTENSION
2. INTRAHEPATIC PORTAL HYPERTENSION

    A. PRESINUSOIDAL

PARENCHYMATOUS PORTAL HYPERTENSION

    B. SINUSOIDAL

    C. POST SINUSOIDAL BLOCK

3. POST HEPATIC PORTAL HYPERTENSION

COLLATERAL CIRCULATION

OESOPHAGEAL VARICES

The porto systemic collateral circulation develops and expand in response to elevation of the portal pressure. Low volume blood flow that normally perfuse these collaterals and flow toward the portal circulation is reversed in portal hypertension because the increased portal pressure exceeds systemic venous pressure. Therefore, flow is reversed in these

collateral vessels and blood flows out of the portal circulation toward the systemic venous circulation.

The important sites of collateral formation are distal oesophagus, proximal stomach, rectum, umbilicus and retro peritoneum.

OESOPHAGEAL VARICES

Four distinct zones of venous drainage at the gastroesophageal junction are particularly relevant to the formation of oesophageal varices.[7]

1. The gastric zone, which extends for two to three centimetrers below the gastroesophageal junction, comprises veins that are longitudinal and located in the submucosa and lamina propria. They come together at the cardia of the stomach and drain into short gastric and left gastric veins.

2. The palisade zone extends two to three centimeters proximal to the gastric zone into the lower end of esophagus. Veins in this zone run longitudinally and in parallel in four groups corresponding to the mucosal folds of oesophagus.

These veins join with veins in the lamina propria. The perforating veins in the palisade zone do not communicate with extrinsic periesophageal veins in the distal esophagus. The palisade zone is the dominant watershed area between the portal and systemic circulations.

3. The third is the perforating zone which is situated more proximal to the palisade zone in the oesophagus, where there is a network of veins. These veins are less likely to be longitudinal and are termed perforating veins because they connect the veins in the oesophageal submucosa and the external veins.

4. The truncal zone, which is the longest zone, is approximately ten centimeters in length, located proximally to the perforating zone in the oesophagus, and usually characterized by four longitudinal veins in the lamina propria.

Veins in the palisade zone in the oesophagus are most prone to bleeding because no perforating veins at this level connect the veins in the submucosa with the peri oesophageal veins. Varices in the truncal zone are unlikely to bleed because the perforating vessels communicate with the peri oesophageal veins, allowing the varices in the truncal zone to decompress. The peri oesophageal veins drain into the azygous system,

and as a result an increase in azygous blood flow is a hallmark of portal hypertension.

The venous drainage of the lower end of the oesophagus is through the coronary vein, which also drains the cardia of the stomach, into the portal vein.

The fundus of the stomach drains through short gastric veins into the splenic vein. In the presence of portal hypertension, varices may therefore form in the fundus of the stomach. Splenic vein thrombosis usually results in isolated gastric fundal varices. Because of the proximity of the splenic vein to the renal vein, spontaneous splenorenal shunts may develop and are more common in patients with gastric varices than in those with oesophageal varices.

Oesophageal varices are formed only when the HVPG exceeds 10 mm Hg and bleeding occurs usually when the HVPG exceeds 12 mm Hg[8]. However not all patients who have a HVPG greater than 12 mm Hg bleed. Other local factors that increase the oesophageal variceal wall tension are required. The varices rupture when the tolerated wall tension is exceeded because the variceal wall gets thinned out and the varices increase in diameter and has an increased pressure.

Larger varices situated at the sites of limited soft tissue support such as the gastroesophageal junction, are at the greatest risk for variceal rupture and variceal bleeding in cirrhotic patients who have portal hypertension. Bleeding from ruptured oesophageal and gastric varices is the most severe complication of cirrhosis and is the important cause of death in about one third of cirrhotic patients. The larger the variceal size the more likely it is to bleed.

Varices usually appear white and opaque . Red colour correlates with blood flow through the dilated sub epithelial and communicating veins. Dilated sub epithelial veins may appear as raised cherry red spots and red wale markings (longitudinal dilated veins resembling whip marks). They lie on top of large subepithelial vessels. The hematocystic spot is approximately 4 mm in diameter. It represents the blood coming from the deeper extrinsic veins of the oesophagus straight out towards the lumen through a communicating vein into the more superficial sub mucosal veins. Red colour is usually associated with larger varices. All the above said signs are associated with a higher risk of variceal bleeding.

Oesophageal varices develop in five to fifteen percent of cirrhotic patients per annum and enlarge by 4 % to 10% per annum. Most patients

who have cirrhosis develop varices, but only one third of the patients experience variceal rupture and bleeding.

Risk factors for variceal bleeding are as follows:

- HVPG greater than 12 mm Hg
- Large oesophageal varices greater than 5 mm
- Red signs
- Child-Pugh class C cirrhosis
- Tense ascites.

When all the above factors are combined and studied they reasonably predict the risk of variceal bleeding[9]. Oesophageal varices with a high risk of bleeding include small varices in child-pugh class C patients and large varices irrespective of child pugh class.

Bleeding from oesophageal varices stops spontaneously in up to 40% of patients. Despite improvements in the management of variceal bleed over the last decade, oesophageal variceal bleeding is associated with a mortality of at least twenty percent at six weeks[10].

It is essential to identify and prophylactically treat high-risk patients because each episode of variceal hemorrhage carries a 15% to 20% mortality, and up to 70% of untreated patients die within 1 year of the initial bleeding episode.

All cirrhotic patients should undergo diagnostic endoscopy to document the presence of varices and to assess their risk for variceal haemorrhage. In patients who have cirrhosis without varices or with varices that do not require intervention, endoscopy must be periodically repeated.

Patients who have cirrhosis without varices should be rescreened at 2 to 3year intervals. Patients who have cirrhosis with small varices that do not warrant therapy should be rescreened at 1 to 2 year intervals[1].

Patients who have Child class B or C with varices of any grade or Child class A with small varices should be considered for primary prophylaxis of variceal haemorrhage.

GASTRIC VARICES

Gastric varices are classified primarily by location. They are classified and described by Sarin et al as follows[11]:

1. Gastroesophageal varices (GOVs): gastric varices in continuity with esophageal varices:

i) Type 1 (GOV1): Along the lesser curve (usually 2–5 cms in length)

ii) Type 2 (GOV2): Along the greater curve extending towards the fundus of the stomach.

2. Isolated gastric varices (IGVs):

i) Type 1 (IGV1): Isolated cluster of varices in the fundus of the stomach

ii) Type 2 (IGV2): Isolated gastric varices in other parts of the stomach.

The likelihood of bleeding from gastric varices depends on their location . Although GOV1 varices constitute over 70% of gastric varices, only 11% of gastroesophageal varices ever bleed. In contrast, about 80% of IGV1 varices experience hemorrhage even though they represent only 8% of all gastric varices. Bleeding from IGV1 varices is often associated with lower portal pressures than in nonbleeding subjects with oesophageal varices. Furthermore, bleeding from such varices is more

severe and the risk of encephalopathy is higher than in patients with bleeding oesophageal varices. Overall, gastric varices bleed less frequently but more severely than oesophageal varices.

PORTAL HYPERTENSIVE GASTROPATHY

Portal hypertensive gastropathy (PHG) is a gastric mucosal change associated with portal hypertension .The “mosaic pattern” and the “cherry red spots” are the most frequently observed elementary lesions in PHG. The former consists of multiple erythematous areas outlined by a white reticular network and is generally considered as “mild” PHG.

The latter are round, red lesions, slightly raised over the surrounding hyperemic mucosa. These carry a higher bleeding risk and are considered to reflect “severe” PHG[12]. The gastric mucosal changes of PHG are associated with increased gastric mucosal and submucosal perfusion and, therefore, are hyperemic not congestive changes.

During the diagnosis of cirrhosis, the prevalence of PHG is approximately 30% and its incidence is approximately 12% per year[13]. However, patients with severe liver dysfunction and large oesophageal varices are at higher risk of developing PHG, whereas large fundal varices may have a protective role, particularly when they are associated

with spontaneous gastrorenal shunt. Overall, during the course of cirrhosis, mild PHG may be observed in up to 50–70% of patients and severe PHG in 20–40%[13].

Endoscopic variceal sclerotherapy or variceal banding is a risk factor for PHG. The clinical course of PHG is characterized by overt or chronic gastric mucosal bleeding. The incidence of overt bleeding from any source in patients with mild PHG is approximately 5% per year, as compared to 15% for severe PHG.

The source of bleeding is the gastric mucosa in most of these bleeding episodes. Overt bleeding from PHG is usually manifested by melena and has a far better prognosis than variceal bleeding, with less than 5% mortality per episode. Mortality is higher in patients with severe PHG, but this has been found to be dependent on the severity of liver dysfunction[13].

The incidence of minor mucosal blood loss, without overt bleeding, is approximately 8% per year in patients with mild PHG and up to 25% in those with severe PHG, in whom severe chronic iron deficiency anemia may result, requiring frequent hospital admissions and blood transfusions.

It appears that the wide use of beta blockers in patients with cirrhosis is reducing both chronic and overt bleeding from PHG because it has been proved that beta blockers significantly reduce the rebleeding risk in patients who have bleeding from PHG .

GASTRIC ANTRAL VASCULAR ECTASIA

Gastric antral vascular ectasia [GAVE] is distinct entity that may be found in association with conditions other than cirrhosis, such as scleroderma or chronic gastritis. GAVE is characterized by aggregates of red spots, usually with a radial distribution from the pylorus in the antrum of the stomach (watermelon stomach).

The histology of GAVE is characterized by marked dilatation of capillaries and collecting venules in the gastric mucosa and submucosa, with areas of intimal thickening in fibromuscular hyperplasia, fibrohyalinosis, and thrombi. From a clinical point of view, GAVE behaves as severe PHG, but it may be less responsive to beta blocker treatment.

CLINICAL FEATURES OF PORTAL HYPERTENSION

SYMPTOMS

Abdominal distention

Vomiting of blood

Altered mental status

Pain abdomen

Fresh or altered blood in stools.

Physical examination

Prominent distended veins in the anterior abdominal wall

Periumbilical collaterals

Rectal hemorrhoids

Ascites - Shifting dullness and fluid thrill

Inguinal and umbilical hernia

Signs of liver cell failure:

Jaundice

Malnutrition

Spider angiomas

Gynaecomastia

Dupuytren's contracture

Muscle wasting

Palmar erythema

Ascites

Splenic enlargement

Atrophy of testis

Asterixis

Hyperdynamic circulatory features.

INVESTIGATION OF PORTAL HYPERTENSION

BLOOD INVESTIGATIONS

Complete blood count

Platelet count - value of < 150000/mm^3 indicates thrombocytopenia

Liver function tests – to assess severity of the liver disease; reversal of

Albumin : Globulin ratio indicates decompensation.

Prothrombin time - This assess the coagulation abnormality

Viral serologies

Antinuclear antibody [ANA]

Antimitochondrial antibody [AMA]

Antismooth muscle antibody [ASMA]

Serum ferritin and iron binding capacity

Alpha1 antitrypsin deficiency

Cerruloplasmin, 24 hour urinary copper , Keyser Fleischer ring

IMAGING STUDIES

ULTRASONOGRAPHY

Ultrasound examination of the liver with doppler study of the vessels has been used widely to assess patients with portal hypertension. Features suggestive of portal hypertension on ultrasonography include splenomegaly (greater than 11 cms), ascites, portosystemic collateral vessels, portal vein diameter greater than 13 mm, splenic vein greater than 11 mm, restricted respiratory modulation of the vascular width. Ultrasound examination can detect thrombosis of the portal vein, which appears as non visualization or cavernous transformation of the portal vein; the latter finding indicates an Extensive collateral network in place of the portal vein. Splenic vein thrombosis also can be demonstrated.

DOPPLER ULTRASONOGRAPHY

Doppler ultrasonography is a non invasive tool to measure the haemodynamics of portal hypertension in cirrhosis and its responsiveness to medical treatment. Although many positive evidences have been suggested, its clinical usefulness in portal hypertension remains unsettled due to lack of reproducibility and accuracy characterized by intra and inter observer variation. However, recently, Doppler's usefulness in assessment of severity of portal hypertension in terms of reproducibility,

technical ease and accuracy and response to drugs that reduce the portal pressure has been proposed.

Blood velocity

Doppler examinations allow the measurement of blood velocity and flow in vessel. This method is simple and confers technical ease that its clinical application in portal hypertension has been attempted. During the measurement of velocity, the angle between the Doppler beam and the long axis of vessel should be less than 60 degrees for accuracy[14,15].

Applications of measuring blood velocity and flow are almost always possible at portal and splenic veins; however at the artery, it is impossible, except at the superior mesenteric artery. To obtain portal vein velocity (PVV), the portal vein is imaged longitudinally in the supine position, and the Doppler sample volume is set at its crossing point with the hepatic artery. When the sample point is adjusted to the centre of the portal vein, the PVV is recorded in a suspended expiration and is averaged over a few seconds. The mean PVV in cirrhotic patients is relatively low compared with that in healthy subjects because of increased intrahepatic vascular resistance (outflow resistance).

Resistance by measuring resistive and pulsatility index

Regardless of the incidence angle, the resistances in the hepatic, splenic artery can be evaluated by measuring the resistive index (RI) and pulsatility index (PI) if the vessel is identified by colour Doppler.

For measuring RI and PI of the hepatic artery, under the right intercostal scanning of the liver, the branch of the hepatic artery around the portal hilus is identified using colour doppler. After the doppler sample volume is located in the branch of the hepatic artery, the time–velocity wave of the doppler signal is recorded. The peak systolic velocity, the end diastolic velocity and the mean velocity are measured.

From these measurements, the hepatic RI [(Peak systolic velocity - End diastolic velocity)/Peak systolic velocity is calculated[16]. The hepatic pulsatile index is calculated as [(Peak systolic velocity – End diastolic velocity)]/Mean velocity.

Pulsatility index is different from resistive index in that it uses mean velocity as its denominator instead of the peak velocity like resistive index. PI is superior to RI when arterial resistance is extremely high that the end diastolic velocity is close to zero.

Colour doppler allows the identification of the main branches of the splenic artery at the splenic hilus[17]. The time–velocity wave is recorded after the Doppler sample volume is placed inside these vessels and the RI and PI are determined using the same method used for the hepatic artery.

Hepatic vein waveform analysis

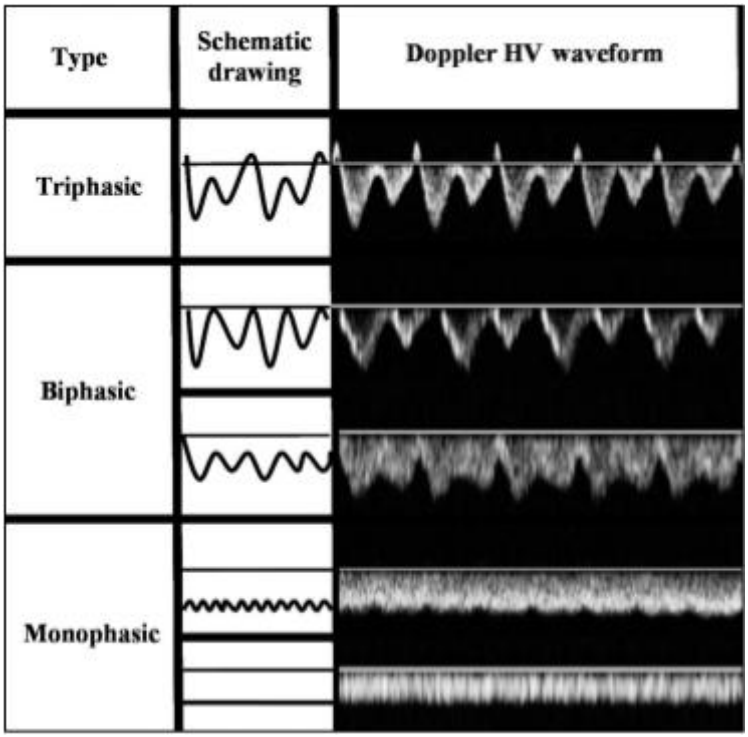
Doppler hepatic vein waveforms in healthy subjects is triphasic (two negative waves and one positive), and the reason for this pattern is the consequence of variations in the central venous pressure because of the cardiac cycle. Biphasic waves have oscillation of positive waves with no negative oscillation. Monophasic waveforms are those which lack phasic oscillation. In cirrhotic patients, the presence of abnormal biphasic or monophasic hepatic vein waveforms has been demonstrated by a number of studies[18,19].

The monophasic hepatic vein waveform is correlated with higher Child–Pugh scores and decreased survival rates in cirrhotic patients[20]. For

doppler hepatic vein examination, hepatic vein is visualized along its longitudinal axis by colour flow doppler mapping in the supine position.

The flow in hepatic vein display the colour of blue in colour flow mapping because flow of the blood is away from the ultrasonic probe used in the doppler study.

Thereafter, doppler shift signals are obtained from the hepatic vein at a distance of three to six centimetres from the junction of the hepatic vein with the inferior vena cava.



The exact cause of the changes in the doppler waveform of the hepatic vein still remains vague. Some investigators have suggested that the hepatic vein wall is thin and it is surrounded by liver tissue and the hepatic compliance is reduced by parenchymal fibrosis and deposition of fat [21].

However, the improvement seen with the vasoactive drug therapy in the hepatic vein waveforms suggests that a haemodynamic effect of high portal pressure, rather than a fixed structural abnormality, is the important pathogenic mechanism responsible for the abnormal waveforms[22].

BARIUM STUDIES

Oesophageal varices appears as filling defects with a smooth contour in the lower third of the esophagus. Uphill and downhill varices can be clearly demonstrated with barium studies. Patients with portal hypertensive gastropathy have thickened gastric folds, which had a mean thickness of 10 mm .The thickened folds had a nodular appearance with undulating contours and indistinct borders which is somewhat different from those of gastric varices, which classically appear as multiple rounded submucosal nodules or as serpentine folds in the gastric fundus.

COLOUR DOPPLER ENDOSCOPIC ULTRASOUND

Colour Doppler endoscopic ultrasound (CD EUS) can provide significant information regarding haemodynamics as well as morphological change in varices. Morphological and haemodynamic

changes of the azygous vein and the left gastric vein occur in patients with portal hypertension. Haemodynamic study and visualization of the azygous vein and the left gastric vein can be performed well with CD EUS to assess portal hypertension.

It has been suggested that a higher hepatofugal flow of the left gastric vein with CD EUS is associated with the development of oesophageal varix[23]. Maximal blood velocity of the azygous vein is increased in patients with portal hypertension.

Azygous vein flow has been found to be four to six times higher in patients with portal hypertension and cirrhosis than in normal subjects and is directly related to pressure in the portal system. CD EUS is also useful in assessing azygos blood flow and in monitoring the effect of vasoactive agents in portal hypertension[24].

MAGNETIC RESONANCE ELASTOGRAPHY

It is a novel method proposed to evaluate liver stiffness. The measurement is obtained by synchronizing motion-sensitive imaging sequences with the application of acoustic waves in tissue media. Preliminary results support its practicability in predicting the stage of fibrosis in patients with cirrhosis [25]. MR elastography has technical

advantages over Fibroscan (no need for an acoustical window, a freely oriented field of view, and the insensitivity to obesity), but it is much more expensive and time consuming

ENDOSCOPIC VIDEOCAPSULE

Patients are frequently intolerant to repeated conventional endoscopies, and often require sedation. Recently, endoscopic videocapsule has been suggested, as this may improve patients tolerance. Once swallowed, the videocapsule records images at predetermined intervals. In a series of published studies, capsule endoscopy allowed a correct identification of varices in 80% of cases[26,27].

However, it may not be as good in assessing variceal size and it may have poor accuracy in identifying the presence of hypertensive gastropathy and gastric varices[27]. Therefore, endoscopic videocapsule cannot be currently recommended as the routine screening method for the evaluation of gastroesophageal varices or portal hypertensive gastropathy in cirrhosis.

OESOPHAGO GASTRO DUODENOSCOPY

The most common and best method of detecting varices is oesophago gastroduodenoscopy. Endoscopic grading of oesophageal

varices is subject to variations. Various criteria have been used to standardize the reporting and grading of oesophageal varices. The best known of these criteria are those compiled by the Japanese Research Society for Portal Hypertension[28]. The descriptors of the varices include red colour signs, colour of the varix, size of the varix, and location of the varix. The colour of the varix can be white or blue.

Varices can be in the lower third, middle third, or upper third of the esophagus. Of all of the aforementioned descriptors, the size of the varices in the lower third of the esophagus is the most important. The size of the varices in the lower third of the esophagus is determined during withdrawal of the endoscope. As much air as possible should be aspirated from the stomach while the esophageal lumen is fully inflated.

Small varices are those which are less than 5 mm in diameter, whereas large varices are greater than 5 mm in diameter[1]. As a point of reference, any varix larger in diameter than an open pinch biopsy forceps is likely to be greater than 5 mm in diameter. This provides a relatively simple and easily reproducible classification. Patients with large oesophageal varices, Child-Pugh class C cirrhosis, and red colour signs on varices have the highest risk of variceal bleeding within 1 year. The increase in bleeding risk attributable to the presence of red color signs,

however, is not independent of the risk associated with large variceal size.

Therefore, prophylactic treatment to prevent variceal bleeding is recommended in all patients with large oesophageal varices irrespective of the presence or absence of red colour signs.

In patients with cirrhosis the overall incidence of variceal bleeding is about 4% per year. This risk increases to 15% per year in patients with large varices. If the HVPG is substantially reduced (below 12 mm Hg or by more than 20% of baseline levels) there is a marked reduction in the risk of bleeding[29], thus demonstrating that the portal hypertension syndrome might be reversed if portal pressure is sufficiently reduced.

MEASUREMENT OF PORTAL PRESSURE

HVPG measurement is the gold standard technique to evaluate the presence and severity of portal hypertension. Measurement of HVPG at hepatic vein catheterisation is an objective and quantitative equivalent of portal pressure in cirrhosis[30]. HVPG has proved to add prognostic information in many settings, including compensated cirrhosis, acute variceal bleeding and patients awaiting liver transplantation

Portal pressure is most commonly assessed by measuring the hepatic venous pressure gradient (HVPG) by hepatic vein catheterization. The HVPG accurately reflects the portal pressure in both alcoholic and viral cirrhosis. HVPG has to be above 10mmHg for varices to develop and above 12mmHg for variceal bleeding.

Prophylaxis of first variceal bleeding[31]:

- Patients without varices should be screened endoscopically for the appearance of varices every 2–3 years.

- In patients with small varices it is indicated to repeat endoscopy every 1–2 years. The interval should be shortened in patients with HVPGP 10 mm Hg.

- Patients with large varices should be treated with a non-selective beta-blocker if there are no contraindications.

- Patients with small varices with red signs or with advanced liver failure (Child-Pugh C) are at similar risk of bleeding as those with large varices and should be considered for preventive therapy

- Patients with large varices with contraindications to or who cannot tolerate beta blockers should be offered endoscopic band ligation.
- Band ligation might be used as first choice in patients with large varices depending on patient’s preferences and local resources.

AIM AND OBJECTIVES OF THE STUDY

1. To assess the relationship of different hepatic and portal vasculature Doppler parameters, their flow characteristics with oesophageal varices.

2. To study the relation of hepatic vein wave forms with oesophageal varices

3. To correlate the Doppler parameters and hepatic vein wave forms in prediction of large oesophageal varices.

MATERIALS AND METHODS

This prospective study included 52 consecutive patients with liver cirrhosis admitted in our institution , Department of Digestive Health and Diseases, Government Peripheral Hospital, Anna nagar, Chennai -102 which is a major tertiary care centre for liver diseases.

Patients were included in this study after their willingness to undergo necessary investigations. Informed written consent was taken before the enrollment in this study. The period of study is from September 2011 to February 2012.

Ethical committee approval was obtained for the study purpose.

INCLUSION CRITERIA:

1. Patients aged between 18 and 80 years with clinical, laboratory and radiological features of cirrhosis and portal hypertension.

EXCLUSION CRITERIA:

1. Patients on diuretics, beta blockers.

2. Previous surgical interventions for portal hypertension.

3. Previous Endoscopic sclerotherapy/ Endoscopic variceal band ligation therapy / TIPS.

4. Presence of portal vein thrombosis.

5. Presence of hepatocellular carcinoma.

6. Active gastrointestinal bleed on admission.

7. Advanced comorbidity for endoscopy.

Clinical evaluation:

In the study group, diagnosis of cirrhosis was done on the basis of clinical, laboratory and radiological parameters. The grading of ascites was done as mild, moderate and severe and the grading of hepatic encephalopathy was done by applying West Haven criteria.

Laboratory Investigations :

Haematological investigations like haemoglobin, WBC count, platelet count, prothrombin time, bilirubin (total, direct, indirect), total protein albumin and globulin, alanine aminotransferase, aspartate aminotransferase, HBsAg and Anti HCV were performed for all patients. Tests for autoimmune liver disease, haemochromatosis and Wilson disease were done only if clinical situation warranted the study. Ascitic fluid analysis was done for estimation of serum ascites albumin gradient. Child pugh score was calculated using the clinical and laboratory parameters.

DOPPLER ULTRASOUND

The patients in the study group were kept under overnight fasting. The Doppler ultrasound was done with the patient in the supine position during quiet respiration. The following Doppler factors were recorded by the same equipment (with a 3 - 5 MHz curvilinear linear - array transducer) and by the same operator for all patients.

(1) Portal vein flow velocity as time average maximal velocity in cm/s [32]

(2)Portal vein diameter

(3) Portal vein cross sectional area

(4)Hepatic artery resistance index (systolic velocity - end diastolic velocity)/systolic velocity];

(5) Splenic artery RI measured (systolic velocity - end diastolic velocity)/systolic velocity

(6) Hepatic artery pulsatility index - (systolic velocity - end diastolic velocity)/ mean systolic velocity[33]

(7) spleen size as length in its longest axis

The following indices were calculated:

(1) Liver vascular index as the ratio of portal venous velocity to hepatic

arterial pulsatility index[34]

(2) Congestion index (CI) of the portal vein was calculated by dividing portal vein cross-sectional area by mean portal vein velocity[35]. Mean velocity was calculated as the time-averaged maximal velocity multiplied by 0.57

The hepatic vein wave forms were measured in the right hepatic vein (RHV) since it drains into inferior venacava in about 85% cases[36]. Doppler waveforms were divided into three types namely triphasic, biphasic and monophasic.

Ascites

Presence of ascites was determined clinically as well as by ultrasound.

Endoscopic features

All the patients were subjected to oesophagoduodenoscopy after an overnight fasting. Oesophageal varices were graded as small if they are less than 5 mm and large if they are greater than 5 mm[1]. Red signs if present were noted over the oesophageal varices.

Gastric varices if present, were typed according to their position and graded as small if less than 10 mm, medium if size is between 10 to 20 mm and large if greater than 20 mm. Portal hypertensive gastropathy was graded as mild and severe.

Hepatic encephalopathy

Grading of hepatic encephalopathy was done based on West Haven criteria[37]. The West Haven scale establishes four stages of hepatic encephalopathy according to alterations in the state of consciousness, intellectual function, behaviour, and neuromuscular signs. The scale includes multiple manifestations for each stage, but lacks specific definitions.

STATISTICAL ANALYSIS

Data were analyzed with SPSS version 15. Descriptive statistics including means, standard deviations, and frequencies were analysed. The chi square test was used to compare differences. Values were considered significant if $P < 0.05$ (95% CI). Presence and grade of oesophageal varices was predicted using the logistic regression equation

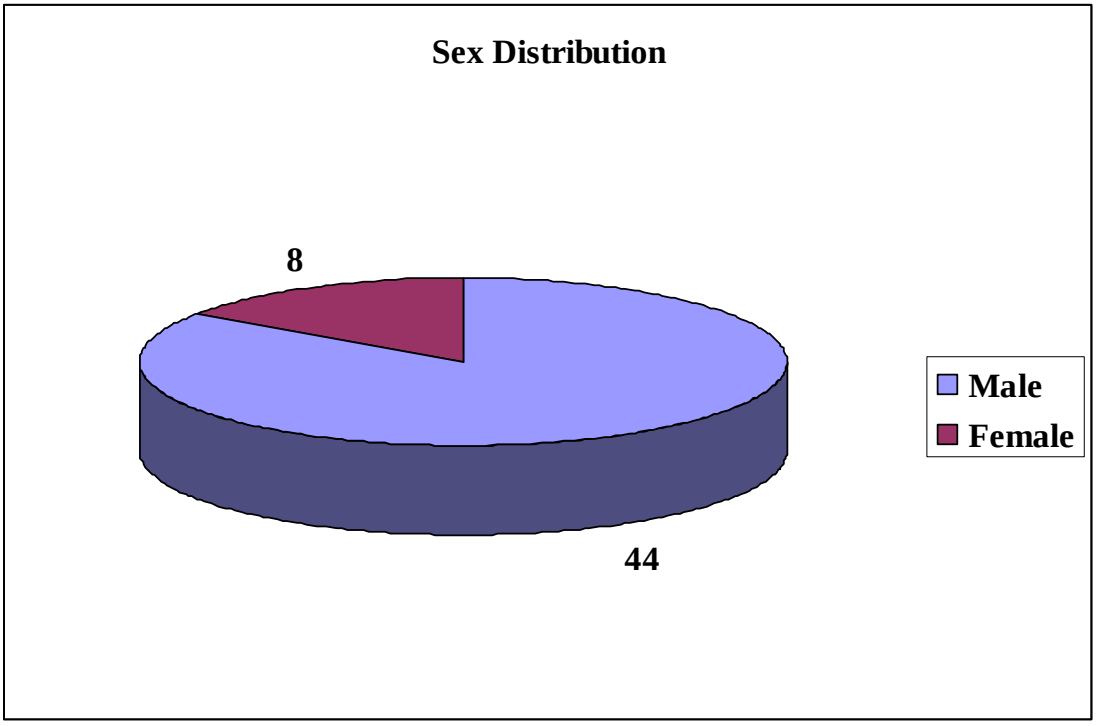
RESULTS

Patient characteristics

A total number of fifty two[52] patients were included in the study. Of those, 44(84.6%) were male and 8 (15.4%) were female. The preponderance of male in this study group was attributed to the etiology of the cirrhosis the most common being ethanol induced.

TABLE 1. SEX DISTRIBUTION OF STUDY POPULATION

		Frequency	Percent
Valid	Male	44	84.6
	Female	8	15.4
	Total	52	100.0



The symptom duration in the patients varies between 15 to 90 days. Ascites was clinically present in 41 of patients and jaundice was present in 30 of patients. About 37 patients had hepatic encephalopathy at presentation.

TABLE 2 : ASCITES

		Frequency	Percent
Valid	Absent	11	21.2
	Present	41	78.8
	Total	52	100.0

TABLE 3 : JAUNDICE

		Frequency	Percent
Valid	Absent	22	42.3
	Present	30	57.7
	Total	52	100.0

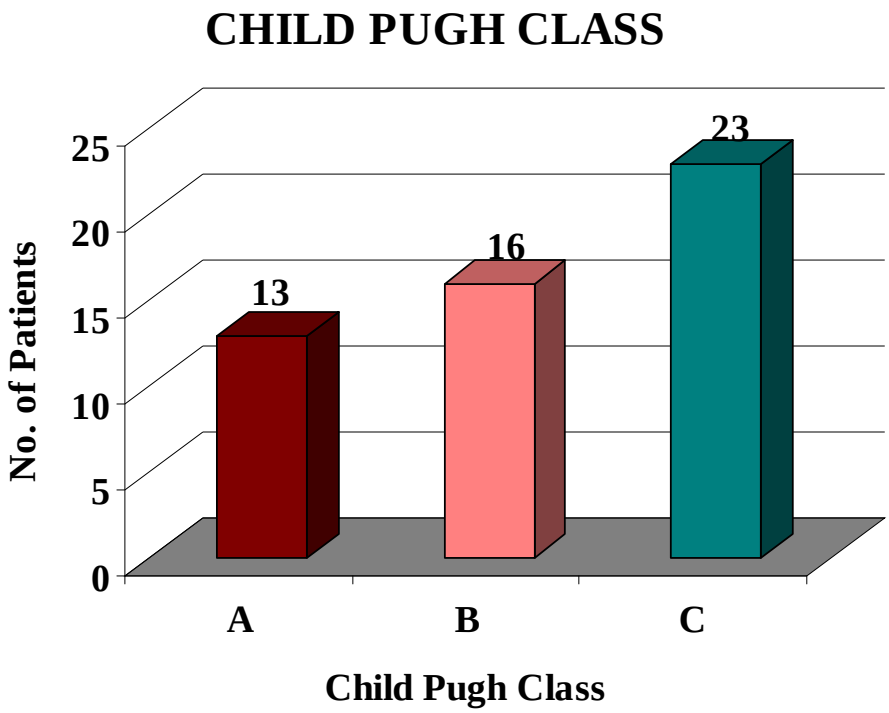
TABLE 4 : HEPATIC ENCEPHALOPATHY

		Frequency	Percent
Valid	Absent	40	76.9
	Present	12	23.1
	Total	52	100.0

The majority of the patients were Child Pugh class C 23 (44.2%). Patients with Child Pugh A were 13 (25%) and Child Pugh B constituted 16 (30.8%) the rest of the study group.

TABLE 5 : CHILD PUGH CLASS IN STUDY POPULATION

		Frequency	Percent
Valid	A	13	25.0
	B	16	30.8
	C	23	44.2
	Total	52	100.0



Oesophageal varices were present in 50 patients of which 31 had small varices (59.6%) and 19 (36.5%) had large varices . Gastric varices was present only in 3 (5.8%) patients.

TABLE 6 : FREQUENCY OF OESOPHAGEAL VARICES IN STUDY GROUP

		Frequency	Percent
Valid	NO VARIX	2	3.8
	Small	31	59.6
	Large	19	36.5
	Total	52	100.0

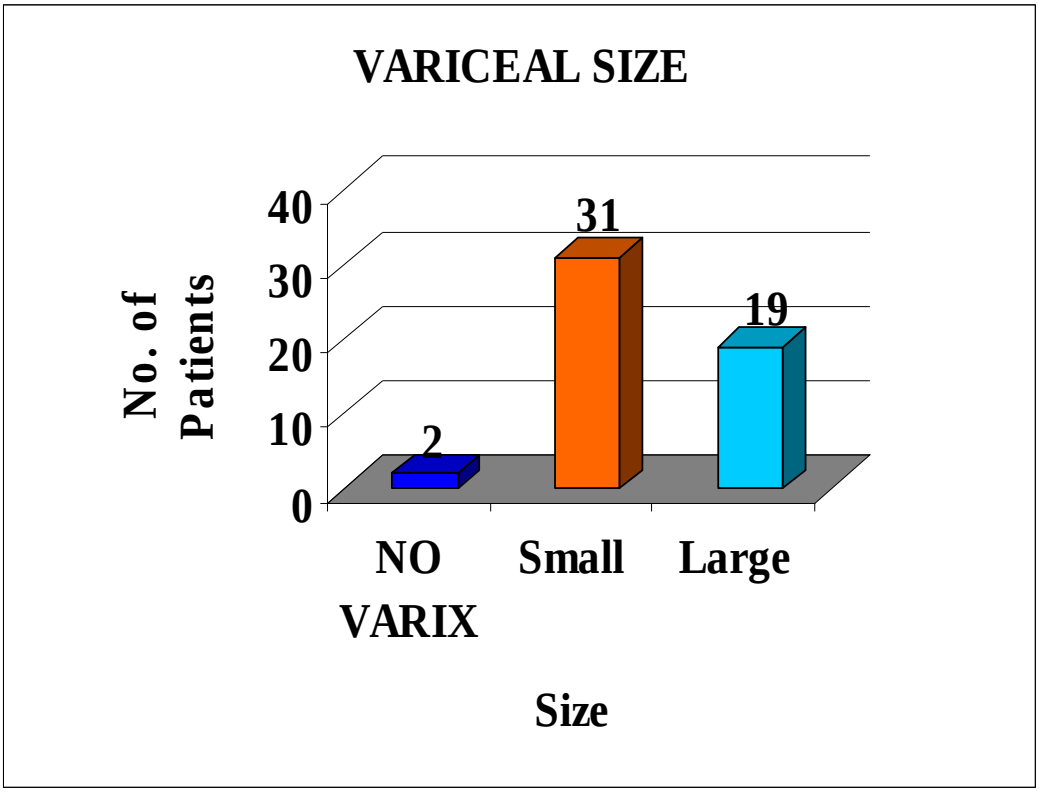


TABLE 7 : FREQUENCY OF GASTRIC VARICES

		Frequency	Percent
Valid	Absent	49	94.2
	Present	3	5.8
	Total	52	100.0

34 patients had portal hypertensive gastropathy, among which 4 (7.7%) had severe and the rest of 30 (57.7%) had mild grade.

TABLE 8 : FREQUENCY OF PORTAL HYPERTENSIVE GASTROPATHY

		Frequency	Percent
Valid	Absent	18	34.6
	Mild	30	57.7
	Severe	4	7.7
	Total	52	100.0

The majority of patients in this study were belong to alcoholic cirrhosis which constitutes of about 63.4%, Hepatitis B - 19.2%, Hepatitis C - 1.9%

TABLE 9: ETIOLOGY OF CIRRHOSIS

		Frequency	Percent
	ALCOHOL	33	63.4
	CRYP	8	15.3
	HBV	10	19.2
	HCV	1	1.9
	Total	61	100.0

Small oesophageal varices were associated with monophasic wave forms in 19.4%. biphasic wave forms in 38.7%, triphasic wave forms in 41.9%. Large oesophageal varices were associated with monophasic wave forms in 42.1%. biphasic wave forms in 52.6%, triphasic wave forms in 6.3%. The p- value was statistically significant with 0.013 [$p < 0.05$].

TABLE 10: CORRELATION OF HEPATIC VEIN WAVE FORMS WITH O. VARICES

			HEP.VEIN WAVEFORMS			Total
			Mono	Bi	Tri	
ESO VARIX	NO VARIX	Count	0	0	2	2
		% within ESO VARIX	.0%	.0%	100.0%	100.0%
		% within HEP.VEIN WAVEFORMS	.0%	.0%	12.5%	3.8%
	Small	Count	6	12	13	31
		% within ESO VARIX	19.4%	38.7%	41.9%	100.0%
		% within HEP.VEIN WAVEFORMS	42.9%	54.5%	81.3%	59.6%
	Large	Count	8	10	1	19
		% within ESO VARIX	42.1%	52.6%	5.3%	100.0%
		% within HEP.VEIN WAVEFORMS	57.1%	45.5%	6.3%	36.5%
Total		Count	14	22	16	52
		% within ESO VARIX	26.9%	42.3%	30.8%	100.0%
		% within HEP.VEIN WAVEFORMS	100.0%	100.0%	100.0%	100.0%

TABLE 11: CORRELATION OF HEPATIC VEIN WAVE FORMS WITH GASTRIC VARICES

			HEP.VEIN WAVEFORMS			Total
			Mono	**Bi**	**Tri**	
GASTRIC V	Absent	Count	13	21	15	49
		% within GASTRIC V	26.5%	42.9%	30.6%	100.0%
		% within HEP.VEIN WAVEFORMS	92.9%	95.5%	93.8%	94.2%
	Present	Count	1	1	1	3
		% within GASTRIC V	33.3%	33.3%	33.3%	100.0%
		% within HEP.VEIN WAVEFORMS	7.1%	4.5%	6.3%	5.8%
Total		Count	14	22	16	52
		% within GASTRIC V	26.9%	42.3%	30.8%	100.0%
		% within HEP.VEIN WAVEFORMS	100.0%	100.0%	100.0%	100.0%

p-value was not significant for gastric varices and portal hypertensive gastropathy.

TABLE 12: CORRELATION OF HEPATIC VEIN WAVE FORMS WITH PORTAL HYPERTENSIVE GASTROPATHY

			HEP.VEIN WAVEFORMS			
			Mono	**Bi**	**Tri**	**Total**
PHG	Absent	Count	2	9	7	18
		% within PHG	11.1%	50.0%	38.9%	100.0%
		% within HEP.VEIN WAVEFORMS	14.3%	40.9%	43.8%	34.6%
	Mild	Count	10	12	8	30
		% within PHG	33.3%	40.0%	26.7%	100.0%
		% within HEP.VEIN WAVEFORMS	71.4%	54.5%	50.0%	57.7%
	Severe	Count	2	1	1	4
		% within PHG	50.0%	25.0%	25.0%	100.0%
		% within HEP.VEIN WAVEFORMS	14.3%	4.5%	6.3%	7.7%
Total		Count	14	22	16	52
		% within PHG	26.9%	42.3%	30.8%	100.0%
		% within HEP.VEIN WAVEFORMS	100.0%	100.0%	100.0%	100.0%

TABLE 13: CORRELATION OF HEPATIC VEIN WAVE FORMS WITH CHILD PUGH SCORE

			CPS			**Total**
			A	**B**	**C**	
HEP.VEIN WAVEFORMS	Mono	Count	3	5	6	14
		% within HEP.VEIN WAVEFORMS	21.4%	35.7%	42.9%	100.0%
		% within CPS	23.1%	31.3%	26.1%	26.9%
	Bi	Count	3	6	13	22
		% within HEP.VEIN WAVEFORMS	13.6%	27.3%	59.1%	100.0%
		% within CPS	23.1%	37.5%	56.5%	42.3%
	Tri	Count	7	5	4	16
		% within HEP.VEIN WAVEFORMS	43.8%	31.3%	25.0%	100.0%
		% within CPS	53.8%	31.3%	17.4%	30.8%
Total		Count	13	16	23	52
		% within HEP.VEIN WAVEFORMS	25.0%	30.8%	44.2%	100.0%
		% within CPS	100.0%	100.0%	100.0%	100.0%

TABLE 14 : DESCRIPTIVE STATISTICS OF LAB VARIABLES ASSOCIATED WITH PRESENCE OF OESOPHAGEAL VARICES

		Sum of Squares	df	Mean Square	F	Sig.
PLT. COUNT	Between Groups	800566507.771	2	400283253.885	.303	.740
	Within Groups	646804142 61.460	49	1320008454.316		
	Total	654809807 69.231	51			
S.Bb	Between Groups	222.375	2	111.187	3.879	.027
	Within Groups	1404.673	49	28.667		
	Total	1627.048	51			
ALBUMIN	Between Groups	.644	2	.322	.737	.484
	Within Groups	21.393	49	.437		
	Total	22.037	51			
INR	Between Groups	1.228	2	.614	3.611	.034
	Within Groups	8.332	49	.170		
	Total	9.560	51			
SAAG	Between Groups	.172	2	.086	.274	.762
	Within Groups	12.536	40	.313		
	Total	12.708	42			

Among the laboratory variables, serum bilirubin and INR had statistical significance with p-value < 0.05

Spleen size greater than 15.3 was associated with large oesophageal varices which was statistically significant. P<0.05

TABLE 15: SPLEEN SIZE ASSOCIATION WITH PRESENCE OF OESOPHAGEAL VARICES

	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	34.833	2	17.417	3.812	.029
Within Groups	223.874	49	4.569		
Total	258.707	51			

TABLE 16 : DESCRIPTIVE STATISTICS OF DOPPLER VARIABLES ASSOCIATED WITH PRESENCE OF ESOPHAGEAL VARICES

		Sum of Squares	df	Mean Square	F	Sig.
PV DIA	Between Groups	6.040	2	3.020	.337	.716
	Within Groups	439.623	49	8.972		
	Total	445.662	51			
	Within Groups	223.874	49	4.569		
	Total	226.107	51			
HARI	Between Groups	.006	2	.003	.567	.571
	Within Groups	.268	49	.005		
	Total	.275	51			
HAPI	Between Groups	.458	2	.229	2.005	.146
	Within Groups	5.602	49	.114		
	Total	6.060	51			
	Within Groups	.327	49	.007		
	Total	.340	51			
PORTAL VEIN VEL	Between Groups	92.255	2	46.128	2.568	.087
	Within Groups	880.259	49	17.964		
	Total	972.514	51			
MEAN PV VELOCITY	Between Groups	27.398	2	13.699	2.318	.109
	Within Groups	289.555	49	5.909		
	Total	316.953	51			
PV CS	Between	.773	2	.386	.670	.516

		Sum of Squares	df	Mean Square	F	Sig.
AREA	Groups					
	Within Groups	28.240	49	.576		
	Total	29.013	51			
LIVER INDEX	Between Groups	63.301	2	31.651	1.619	.209
	Within Groups	958.177	49	19.555		
	Total	1021.478	51			
CONG INDEX	Between Groups	.104	2	.052	1.782	.179
	Within Groups	1.424	49	.029		
	Total	1.527	51			

p- value was not statistically significant for the above variables.

TABLE 17: SPLENIC ARTERY RESISTIVE INDEX ASSOCIATION WITH PRESENCE OF OESOPHAGEAL VARICES

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	.211	2	.105	15.770	.000
Within Groups	.327	49	.007		
Total	.538	51			

p-value was significant for SARI. P< 0.0001.

DISCUSSION

Variceal bleeding due to portal hypertension develops in 30 – 40% of patients with cirrhotics. With the growing number of chronic liver disease in the world , the likelihood of patients presenting with gastrointestinal bleeding will increase associated with the concurrent increase in the screening procedures for varices. Non invasive screening for identifying patients with high risk varices will definitely of help by means of reducing the cost and improve patient's tolerability.

Studies conducted on noninvasive predictor of varices[38] lack uniformity in their structure. Moreover the accuracy of prediction of oesophageal varices by these non invasive markers is found to be unsatisfactory and hence lack clinical applicability.

It was estimated that 100 screening endoscopy need to be preformed to prevent 1-2 cases of variceal bleeding .Therefore, identification of clinical features that can accurately predict esophageal varices and help identifying patients at greatest risk is important to improve the yield and cost- effectiveness of endoscopic screening.

In the present study, there was preponderance of male as compared to female. This was expected as the most common cause of cirrhosis was

ethanol [63.4%] and ethanol consumption was common in males. Most of the patients were in the Child Pugh class B & C. This was also to be expected as our unit is a tertiary care centre catering treatment to advanced liver diseases.

In this study, the relationship of the hepatic vein wave forms with oesophageal varices was studied. Small oesophageal varices were associated with monophasic wave forms in 19.4%. biphasic wave forms in 38.7%,triphasic wave forms in 41.9%.

Large oesophageal varices were associated with monophasic wave forms in 42.1%. biphasic wave forms in 52.6%,triphasic wave forms in 6.3%. This had a statistical significance $p<0.05$ and the monophasic waves were associated with large varices. This is in concurrence to previous studies.

Baik et al[22] prospectively examined the relationship between waveforms and the severity of portal hypertension measured by HVPG in 78 cirrhotic patients who experienced variceal bleeding. A correlation was found between abnormalities in HV waveforms and HVPG, i.e. with increasing HVPG, the HV waveform tended to flatten. Furthermore, the monophasic waveform was associated with severe portal hypertension (HVPG 415 mmHg) with relatively high sensitivity and specificity in that

study population. Hence, flattening of the HV waveform observed in the cirrhotic patients indicates a high likelihood of severe portal hypertension.

In a study from South India conducted by Thomas Joseph et al.[39] it was shown that a loss of triphasic wave pattern was associated with large oesophageal varices. The sensitivity of loss of the triphasic wave pattern in detecting significant large varices was very high (95.23%) and negative predictive value was also high (75%). Severity of liver disease as indicated by Child-Pugh and MELD scores did not correlate with changes in hepatic venous waveforms.

Gorka et al[40] in a study found sensitivity for the detection of large varices was 92% for monophasic waves, 76% for waves with loss of the reverse flow component, and 62% for biphasic waves. Overall specificity was 100%.

Kim and colleagues[42] prospectively evaluated the correlation between the extent of abnormal Doppler HV waveforms, expressed as Damping Index [DI], and the HVPG, and response to propranolol in patients with cirrhosis. DI is calculated by dividing the minimum velocity over the maximum velocity of the HV waveform.Abnormal HV waveforms were seen in 66 out of 76 patients (86.8%).

Flattening of the HV wave can be attributed to an increase in HV inflow from intrahepatic shunts implicated in portal hypertension[42]. This results in haemodynamic blunting of the effect of variations in central venous pressure during the cardiac cycle, rather than lack of liver compliance. There was no stastical significant correlation of the hepatic vein wave forms with gastric varices, portal hypertensive gastropathy and red signs on oesophageal varices.

Splenomegaly

Splenomegaly is the cardinal sign of hypertension in cirrhotic patients. Our data showed that spleen size measured by ultrasonography was an independent predictor for the presence of varices.

In our study, spleen size of greater than 15.3 cms was associated with presence of large varices, with a p value of 0.029. [$p<0.05$]

Dib N, et al[43] identified non invasive diagnosis of large oesophageal varices because of prognostic and economic issues. He concluded that Indirect echographic markers of portal hypertension and oesophageal varices (ascites, portal vein diameter > or = 13 mm, spleen length, maximal and mean velocimetry of portal vein flow, respectively

< 20 cm/s and < 12 cm/s) could be useful. Among this parameters, spleen length is an independent predictive marker of oesophageal varices.

In Sharma et al study[44] , 101 patients (median age 45; range 15-74 years; 87 male; Child-Pugh class: A 18, B 31, C 52), 46 had large oesophageal varices. On univariate analysis, five variables were significantly associated with the presence of large varices. These included pallor (P = 0.026), palpable spleen (P = 0.009), platelet count (P < 0.002), total leukocyte count (P < 0.0004) and liver span on ultrasound (P = 0.031). On multivariate analysis, two of these parameters, namely low platelet count and presence of palpable spleen, were found to be independent predictors of the presence of large varices.

In Jeon SW et al study[45] variables associated with the presence of oesophageal varices on univariate analysis were serum albumin, total bilirubin, prothrombin time and platelet count ($p<0.05$). On multivariate analysis, independent variables were platelet count (odds ratio (OR) 0.922; 95% confidence interval (CI), 0.86-0.99), diameter of spleen (OR 5.4; 95% CI, 1.63-17.88) and platelet count/spleen diameter ratio (OR 1.007; 95% CI, 1.01-1.02). The optimal critical value for the diameter of spleen was 11 cm. The sensitivity and specificity with this value were 84% and 63%, respectively.

Doppler parameters of portal vasculature were evaluated for their relation with oesophageal varices. Except for splenic artery resistivity index, none of the other variables were having correlation with oesophageal varices.

In a study by Fabio piscaglia et al[46] portal vein flow velocity and congestion index, hepatic and splenic arteries resistance indexes, modified liver vascular index were measured and studied with relation with oesophageal varices. Highest accuracy was achieved by the splenic artery RI and the portal hypertension index (both around 75%) at cut-offs, respectively, of 0.60 and 12 cm/s. None of the other parameters were having statistical significance.

In another study by Daniel Dutra Cançado[47] In patients with cirrhosis, both splenic indices were higher (RI = 0.63 ± 0.08; PI = 1.02 ± 0.22) than those found in patients with chronic hepatitis (RI = 0.58 ± 0.06; PI = 0.89 ± 0.15) and in the control group individuals (RI = 0.57 ± 0.04; PI = 0.87 ± 0.11). However, cirrhotic patients with evidence of collateral circulation at ultrasound presented lower resistive indices (RI = 0.60 ± 0.08) compared with those without collateral circulation (RI = 0.65 ± 0.07), possibly due to the portosystemic shunt caused by collateral

vessels. There was no significant difference of indices between patients with and without esophageal varices.

Portal flow velocity is decreased in cirrhotic patients. However the absolute values vary significantly in both healthy subjects and cirrhotic patients[48]. In our study, portal vein flow velocity was 10 cms/sec [mean] for large varices , whereas it was 12.8 cms/sec for small varices. There was no significant stastical difference for prediction of large varices.

In a study by Iwao et al[34] the value of portal venous velocity was significantly lower (11.0 +/- 2.4 vs 15.9 +/- 2.8 cm/s, $p < 0.001$) and hepatic arterial pulsatility index was significantly higher (1.28 +/- 0.18 vs 0.95 +/- 0.17,$p < 0.001$) in patients than in controls.

In another study in which portal and splenic haemodynamics were studied[49] portal flow velocity was decreased in cirrhotic patients with Child's C cirrhosis, as compared to those with Child's A cirrhosis ($P < 0.001$).

The portal blood flow volume in Child's C cirrhosis were also significantly low compared to patients with Child's A and Child's B cirrhosis ($P < 0.001$ and $P < 0.05$, respectively). There was a significant increase in the portal vein congestion index and splenic vein congestion

index in patients with Child's C cirrhosis as compared to patients with Child's A cirrhosis (P < 0.001). Among cirrhotic patients, the group with esophageal variceal bleeding had significantly greater splenic blood flow volume and splenic vein congestion index (P < 0.001). Patients with ascites had significantly lower portal flow velocity (P< 0.001) and higher portal vein congestion index and splenic vein congestion index (P = 0.003 and P = 0.05, respectively) as compared to those without ascites

Zironi and colleagues[50] reported that the mean velocity of portal vein in cirrhosis and normal subjects were 13.0 ± 3.2 vs. 19.6 ± 2.6 cm/s respectively. The cut-off value of 15 cm/s showed a sensitivity and specificity of 88 and 96%.

Arved et al[51] showed hepatic arterial pulsatility index was significantly higher in patients with cirrhosis than in controls (0.9220.1 VS. 1.14±0.18; p<0.001) and directly correlated with the hepatic venous pressure gradient.

(r=0.7; p<0.001).

Liver vascular index and congestion index were not statiscally significant in our study. This is in accordance in the previous studies.[46]

In a study by Mohammad K Tarzamni[52] a logistic regression model showed that the parameters like liver vascular index, congestion index were not good predictors of the presence of oesophagogastric varices. This study indicate that using Doppler parameters such as spleen size, splenic artery resistive index, hepatic vein wave forms allows prediction of presence of large oesophageal varices with a fairly high accuracy. Values for the non-invasive indicators from this study and comparables need to be validated in further series studies. Selecting patients for an oesophagoduodenoscopy may be cost effective and will define patients who need a critical management.

CONCLUSION

- This study shows spleen size and splenic artery resistivity index correlate clearly with the presence of large esophageal varices. However these parameters did not predict the presence of gastric or other porto systemic collaterals.

- Presence of hepatic vein monophasic wave forms predicts the incidence of large oesophageal varices.

- This would encourage the use of endoscopy screening in patients with large oesophageal varices and this would help to reduce the burden and cost for the patients and health care providers.

- Studies on large scale are needed before applying these parameters as predictors of oesophageal varices. If so it will enable us to start primary prophylaxis with out subjecting patients to oesophagoduodenoscopy.

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PROFORMA

Name: Age : Sex: Address: MGE No.:

Clinical History & Features:

ABDOMINAL DISTENTION

HE

BLEEDING

JAUNDICE

DIAGNOSIS:

CBC: PLT.COUNT: LFT:

Prothrombin Time:

RFT:

HBs Ag/ Anti HCV:

HIV:

ASCITIC FLUID ANALYSIS:

USG ABDOMEN:

CHILD PUGH SCORE:

ENDOSCOPY: OV: GV: PHG:

Red Signs:

DOPPLER STUDY:

DOPPLER PARAMETRES

1. PORTAL VEIN FLOW VELOCITY
2. PORTAL VEIN DIAMETER
3. PORTAL VEIN CROSS SECTIONAL AREA:
4. HEPATIC ARTERY RESISTANCE INDEX [RI] =

   $$\frac{\text{Systolic velocity – End diastolic velocity}}{\text{Systolic velocity}}$$

5. HEPATIC ARTERY PULSATILITY INDEX:

   $$\frac{\text{Systolic velocity – End diastolic velocity}}{\text{Mean Systolic velocity}}$$

6. SPLENIC ARTERY RESISTIVE INDEX :

   $$\frac{\text{Systolic velocity – End diastolic velocity}}{\text{Systolic velocity}}$$

7. SPLEEN SIZE:
8. HEPATIC VEIN FORMS: MONOPHASIC /BIPHASIC / TRIPHASIC

Liver vascular index = $\frac{\text{Portal venous velocity}}{\text{Hepatic arterial pulsatility index}}$

Congestion index (CI) of PV= $\frac{\text{Portal vein cross-sectional area}}{\text{Mean Portal blood velocity}}$

MASTER CHART

S. NO	NAME	AGE	SEX	MGENO	ASCI-TES	HE	JAUN-DICE	ETIO-LOGY	PLT. COUN	S.BB	ALBU MIN	INR	SAAG	CPS	ESOV-ARIX	PHG	REDS-IGNS	GAST-RICV	HEP. VEIN	PVDIA	SPL-EEN SIZE	HARI	HAPI	SARI	PORT-ALVE	MEAN-PVVE	PVCS-AREA	LIVERIND	CONGINDE
1	JOTHI	70	2	5,856	0	0	0	4	120,000	0.7	4.1	1.2		1	2	0	1	1	3	13.5	15.7	0.79	1.71	0.81	6.79	3.97	2.12	3.97	0.534
2	PUUNIYAMOORTHY	44	1	2,014	1	0	1	1	130,000	5.1	3.8	1.3	3.0	2	2	0	0	0	2	15.3	14.3	0.63	0.90	0.81	11.36	6.40	2.21	12.60	0.345
3	BOOBALAN	56	1	1,212	1	0	0	1	150,000	0.5	2.9	1.3	2.1	2	1	1	0	0	1	17.2	14.4	0.64	1.11	0.59	19.28	10.90	3.23	17.36	0.296
4	JEGAN	33	1	7,528	1	1	1	1	161,000	22.7	3.1	2.5	2.2	3	1	1	0	0	2	9.0	14.0	0.56	0.98	0.67	19.63	11.10	1.06	20.03	0.090
5	SURESH	34	1	131	0	0	0	2	110,000	0.8	3.0	1.1		1	2	1	0	0	1	10.7	17.5	0.77	1.69	0.86	8.57	4.80	0.91	5.07	0.189
6	PRAKASAM	53	1	466	1	0	1	2	80,000	3.2	2.9	1.7	1.9	2	1	1	0	0	3	7.0	15.5	0.76	1.35	0.66	6.43	3.60	0.60	4.70	0.166
7	MOHANDOSS	46	1	6,595	1	1	1	1	210,000	3.4	1.6	2.1	1.1	3	1	0	0	0	2	9.2	9.3	0.64	0.98	0.67	14.70	8.37	1.16	15.00	0.130
8	MURUGAN	40	1	7,332	1	1	1	1	150,000	17.6	2.8	2.2	1.3	3	1	1	0	0	1	9.0	14.6	0.64	1.24	0.64	5.00	2.85	0.85	4.03	0.290
9	MADHUCHANDRAN	34	1	1,468	1	0	0	1	184,000	1.3	2.9	1.8	2.3	2	1	1	0	0	3	17.2	16.0	0.69	1.80	0.76	16.44	9.37	2.19	9.13	0.235
10	ARUMUGAM	52	1	7,436	1	1	1	1	115,000	4.5	1.9	2.0	1.3	3	1	1	0	0	1	10.9	12.1	0.67	1.41	0.71	11.43	6.51	1.08	8.10	0.165
11	DEIVANAI	48	2	4,544	1	0	0	4	140,000	1.2	3.4	1.2	1.8	1	1	1	0	0	1	13.1	12.4	0.76	1.29	0.75	3.80	2.10	2.06	2.94	0.980
12	NAGARAJ	55	1	6,899	1	1	1	1	178,000	8.4	3.5	2.1	2.5	3	1	0	0	0	3	11.7	13.7	0.69	1.33	0.81	13.57	7.73	1.05	10.20	0.135
13	MUNUSWAMY	44	1	3,684	1	0	0	2	190,000	1.1	3.0	1.2	2.1	2	2	1	0	0	1	11.1	17.7	0.76	2.14	0.80	7.15	4.07	1.12	3.34	0.275
14	SURESH	36	1	1,920	1	1	1	1	140,000	3.5	3.1	1.8	1.9	3	2	2	1	0	1	12.0	17.8	0.76	1.49	0.72	9.28	5.20	0.96	6.22	0.184
15	KOTHANDAN	51	1	3,385	0	0	0	2	198,000	0.7	3.0	1.1		1	1	1	0	0	3	13.5	14.5	0.64	1.10	0.75	8.22	4.60	1.74	7.47	0.378
16	SUBRAMANI	59	1	2,878	1	0	0	4	184,000	0.5	4.2	1.1	3.0	1	2	0	0	0	2	4.6	17.7	0.70	1.18	0.80	11.60	6.61	1.13	9.83	0.196
17	VADIVEL	30	1	6,299	1	1	1	1	180,000	10.2	2.5	2.7	2.0	3	1	1	0	0	2	15.7	16.6	0.78	1.73	0.74	17.14	9.70	3.31	9.90	0.340
18	MEER JAMA HUSSAIN	59	1	851	1	0	0	1	160,000	0.3	2.7	1.2	1.7	2	2	1	1	0	2	13.4	12.0	0.83	2.01	0.91	15.71	8.94	2.14	7.81	0.239
19	KARUNAKARAN	50	1	6,066	1	0	0	1	178,000	0.3	3.1	1.4	1.8	2	0	0	0	0	3	12.1	13.3	0.76	1.94	0.74	13.90	7.92	1.44	7.16	0.181
20	PARVEEN	34	2	267	1	0	0	4	140,000	0.7	3.0	1.2	1.3	2	2	0	1	1	2	9.8	19.1	0.76	0.70	0.80	10.14	5.70	0.70	14.40	0.122
21	GURUVAYYA	32	1	6,137	1	0	1	2	150,000	7.3	2.8	1.8	1.6	3	1	0	0	0	3	11.7	15.3	0.77	1.42	0.76	14.28	8.13	1.44	10.05	0.177
22	ARUMUGAM	40	1	2,348	1	0	1	1	190,000	8.3	2.9	1.9	1.7	3	1	1	0	0	2	13.0	13.5	0.79	1.60	0.77	10.00	5.70	1.42	7.46	0.249
23	RAVICHANDRAN	50	1	5,841	1	0	0	1	160,000	1.3	3.9	1.1	2.4	1	1	1	0	0	3	11.7	11.9	0.77	1.42	0.76	14.28	8.13	1.44	10.05	0.177
24	MANIAMMAL	47	2	2,661	1	0	0	4	242,000	0.9	3.0	1.1	1.8	2	2	1	1	1	1	11.5	14.5	0.63	1.09	0.76	5.00	2.85	1.43	4.58	0.500
25	MANI	64	1	6,207	1	1	1	1	170,000	2.0	3.4	2.0	2.3	3	2	1	0	0	2	13.2	13.0	0.76	1.51	0.82	6.43	3.66	1.26	4.20	0.340
26	CHEZHIAN	40	1	6,157	1	0	1	1	160,000	4.6	3.5	1.8	2.2	3	1	0	0	0	2	14.9	12.8	0.60	1.12	0.55	10.10	5.75	1.98	9.00	0.344
27	MURUGESA PANDIAN	27	1	6,559	0	0	0	2	80,000	0.7	3.5	1.3		1	2	0	0	0	1	17.3	19.3	0.72	1.64	0.79	12.86	7.33	3.46	7.84	0.470
28	RAVINDRAN	46	1	7,511	1	0	1	1	110,000	2.6	3.7	1.7	2.3	2	1	0	0	0	2	13.9	14.4	0.78	1.72	0.65	17.14	9.76	2.26	9.96	0.231
29	BHARATHI	35	2	2,290	0	0	1	2	71,000	2.8	3.7	1.1		1	1	0	0	0	2	13.0	17.8	0.65	1.47	0.49	17.14	9.76	1.46	11.65	0.149
30	SARAVANAMUTHU	43	1	6,413	0	0	1	2	182,000	1.9	4.0	1.2		1	2	1	1	0	2	11.3	17.6	0.69	1.45	0.87	11.60	8.00	0.91	8.00	0.137

S. NO	NAME	AGE	SEX	MGENO	ASCI-TES	HE	JAUN-DICE	ETIO-LOGY	PLT. COUN	S.BB	ALBU MIN	INR	SAAG	CPS	ESOV-ARIX	PHG	REDS-IGNS	GAST-RICV	HEP. VEIN	PVDIA	SPL-EEN	HARI	HAPI	SARI	PORT-ALVE	MEAN-PVVE	PVCS-AREA	LIVERIND	CONGINDE
31	SENGUTTUVAN	43	1	1,562	0	0	0	4	160,000	1.1	3.6	1.2		1	0	0	0	0	3	14.0	11.0	0.73	1.72	0.66	12.14	6.91	2.19	7.05	0.316
32	RATHINAVEL	55	1	1,786	1	0	1	3	171,000	2.5	2.0	1.8	1.4	3	2	1	0	0	2	8.5	11.1	0.69	1.31	0.91	19.63	11.18	0.69	14.98	0.061
33	KUMARAVEL	34	1	3,434	1	0	1	1	140,000	3.7	3.9	1.9	2.9	2	1	0	1	0	2	8.3	10.7	0.58	1.00	0.61	16.43	9.36	0.70	16.43	0.074
34	BHUVANESHWARI	31	2	5,182	0	0	0	2	138,000	0.7	4.8	1.2		1	1	0	0	0	3	13.0	17.0	0.85	1.51	0.75	21.00	11.97	1.70	12.60	0.142
35	NACHIMUTHU	43	1	4,111	1	0	1	1	160,000	3.2	3.4	1.5	2.4	3	1	1	0	0	2	13.4	15.5	0.72	1.66	0.71	14.00	7.98	1.58	8.43	0.197
36	NAGARAJ	64	1	4,574	0	0	1	1	140,000	5.6	2.7	1.7	2.2	3	2	2	1	0	1	14.6	14.8	0.57	1.10	0.78	8.57	4.88	2.25	7.72	0.461
37	RAJA	39	1	7,835	1	1	1	1	115,000	19.7	2.6	2.2	2.2	3	1	2	0	0	3	6.1	11.0	0.67	1.06	0.50	14.28	8.13	0.46	13.47	0.050
38	KOTHANDAM	51	1	3,385	0	0	0	2	198,000	0.7	4.5	1.2	0.0	1	1	1	0	0	3	13.5	14.5	0.64	1.10	0.76	8.22	4.68	1.74	7.47	0.371
39	PRAKASAM	53	1	466	1	0	1	1	80,000	2.6	2.9	1.7	2.1	2	1	1	0	0	3	7.7	15.5	0.76	1.35	0.66	6.43	3.66	0.60	4.76	0.163
40	RAJA	46	1	7,826	1	1	1	1	151,000	15.0	2.6	1.1	1.8	3	1	1	0	0	1	13.2	13.6	0.52	0.76	0.44	18.47	10.52	1.04	24.30	0.098
41	RADHA	53	1	694	1	0	0	1	140,000	2.9	5.0	1.2	3.0	2	2	1	0	0	2	13.5	13.9	0.74	2.19	0.75	10.18	5.80	1.83	4.64	0.315
42	MANIVANNAN	51	1	51	1	0	1	1	115,000	20.4	3.0	2.4	2.2	3	1	1	0	0	2	12.5	15.4	0.73	1.73	0.67	8.93	5.09	1.69	5.16	0.332
43	KOKILA	33	2	1,111	1	0	0	4	135,000	0.5	3.2	1.2	1.7	2	1	0	0	0	1	7.9	12.8	0.65	1.46	0.68	12.14	6.90	0.70	8.32	0.101
44	THUKKARAM	45	1	8,143	1	0	1	1	100,000	2.6	2.9	2.1	1.7	3	2	1	1	0	2	12.3	13.2	0.62	1.35	0.76	7.86	4.48	3.56	5.82	0.794
45	VEDHAM	61	2	109	0	0	0	4	199,000	0.6	3.0	1.2		1	1	1	0	0	3	12.0	12.0	0.67	1.18	0.73	8.57	4.88	1.65	7.26	0.338
46	RAJENDRAN	45	1	2,654	1	0	1	1	130,000	15.2	2.6	2.2	2.0	3	1	2	0	0	2	6.3	12.3	0.67	1.06	0.50	14.28	8.13	0.46	13.47	0.056
47	VIJAYAN	52	1	3,452	1	1	1	1	170,000	4.3	3.4	1.8	2.3	3	2	1	0	0	1	13.6	14.5	0.76	1.51	0.82	6.43	3.66	1.26	4.20	0.340
48	SEKAR	50	1	7,511	1	1	1	1	120,000	2.0	3.4	1.8	2.3	3	1	1	0	0	2	13.2	12.0	0.76	1.51	0.72	6.43	3.66	1.26	4.20	0.340
49	NARESH	44	1	5,333	1	0	1	1	150,000	7.3	2.8	1.6	2.2	3	1	0	0	0	3	11.7	15.3	0.77	1.42	0.76	14.28	8.13	1.44	10.05	0.177
50	MAGESH	40	1	4,421	1	0	0	1	184,000	1.3	2.9	1.8	2.3	2	1	1	0	0	3	17.2	16.0	0.69	1.80	0.76	16.44	9.37	2.19	9.13	0.235
51	KARTHICK	49	1	549	1	0	1	1	130,000	5.1	3.8	1.4	1.7	3	2	0	0	0	2	15.3	14.3	0.63	0.90	0.81	11.36	6.40	2.21	12.60	0.345
52	NAGESH	42	1	7,752	1	0	0	1	160,000	0.8	2.9	1.2	1.7	2	2	1	0	0	1	15.3	14.3	0.63	0.90	0.81	11.36	6.40	2.21	12.60	0.345

ABSENT ABS ABSEN ALCOHOL - 1
PRESEN PRE PRESE HBV- 2
HCV-3
CRYPTOGENIC -4

NO VAR ABSE ABSENT ABSEN MONOPHASIC - 1
SMALL - MILD PRESEN PRESEI BIPHASIC -2
LARGE · SEVERE - 2 TRIPHASIC - 3